

To: DeMarini, David[DeMarini.David@epa.gov]; Paul Lambert[plambert@wisc.edu]; Coglian, Vincent[coglian.vincent@epa.gov]; bucher@niehs.nih.gov[bucher@niehs.nih.gov]; Chris Portier[cportier@me.com]; Caldwell, Jane[Caldwell.Jane@epa.gov]; Gibbons, Catherine[Gibbons.Catherine@epa.gov]; Kate Guyton[GuytonK@iarc.fr]; Fritz, Jason[Fritz.Jason@epa.gov]; iir@unc.edu[iir@unc.edu]; lambert@oncology.wisc.edu[lambert@oncology.wisc.edu]; Kavlock, Robert[Kavlock.Robert@epa.gov]; hecht002@umn.edu[hecht002@umn.edu]; Robert Baan[BaanR@iarc.fr]; Kurt Straif[straifk@iarc.fr]; Rusyn, Ivan[IRusyn@cvm.tamu.edu]
Cc: Martyn Smith[martynts@berkeley.edu]
From: Martyn Smith
Sent: Tue 2/10/2015 4:41:11 AM
Subject: Re: Revised Characteristics of Carcinogens Paper
[Key Characteristics of Carcinogens 2-7-15.docx](#)
[Key Characteristics of Carcinogens 2-6-15.docx](#)

Dear all

Following multiple exchanges with a variety of authors I am pleased to circulate a new draft of the Characteristics paper. I have tried to incorporate as many suggestions as possible and have used many of David's very useful edits to the manuscript. I have not however changed the title much and I have kept the term Key Characteristics. I agree that these are Characteristic Properties of Carcinogens but this terminology is too much of a mouthful for me and the term properties is not descriptive enough in my view. I have used the term 'characteristic properties' several times but have dropped biological/biochemical as I think this can be assumed. Vince had suggested Aetiological characteristics but this leads to arguments over spelling and more importantly perhaps causality and so I have not used the term.

Two versions of the paper are attached. The version date 2-6-15 shows all the track changes. These are all accepted in the 2-7-15 version.

I have changed the authorship order according to suggestions by Kurt and Vince and have agreed with them that the Acknowledgements should include all the members of the working group who attended either or both workshops in Lyon in 2012. Kurt will provide this list.

Some of you may be uncomfortable with the arrowed diagrams at the end of the paper but a number of the senior authors agree that going beyond just describing the characteristics is important and that we should describe how they could be used potentially in a mechanistic evaluation. The examples given also come from a very recent IARC monograph and a review on benzene that was used in EPA's NextGen report, so I think we are on fairly solid ground.

The reference list is now fairly complete (I cannot find one by Higgins) but is slightly too long as Carcinogenesis recommends only 50 for its reviews. Suggestions for cuts are welcome. The paper is now 4,926 words in length excluding figures, tables and abstract which fits with the guidelines for Carcinogenesis if we agree that is the best journal for this paper. It also fits with EHP guidelines for that matter.

I welcome your feedback but would like to submit this in the near future rather than make many more lengthy revisions at this point. Please submit the draft to review processes at your institution for approval if you have such a procedure. If I do not hear otherwise I will take it that we all agree that Carcinogenesis is our first choice of journal.

Thanks for all your efforts in bringing this to fruition.

With warm regards,

Martyn

From: "DeMarini, David" <DeMarini.David@epa.gov>

Date: Monday, January 26, 2015 5:46 AM

To: Paul Lambert <plambert@wisc.edu>, "Cogliano, Vincent" <cogliano.vincent@epa.gov>

Cc: "bucher@niehs.nih.gov" <bucher@niehs.nih.gov>, Martyn Smith <martynts@berkeley.edu>, Chris Portier <cportier@me.com>, "Caldwell, Jane" <Caldwell.Jane@epa.gov>, "Gibbons, Catherine" <Gibbons.Catherine@epa.gov>, Kate Guyton <GuytonK@iarc.fr>, "Fritz, Jason" <Fritz.Jason@epa.gov>, "iir@unc.edu" <iir@unc.edu>, "lambert@oncology.wisc.edu" <lambert@oncology.wisc.edu>, "Kavlock, Robert" <Kavlock.Robert@epa.gov>, "hecht002@umn.edu" <hecht002@umn.edu>, Robert Baan <BaanR@iarc.fr>, Kurt Straif <straifk@iarc.fr>

Subject: RE: Revised Characteristics of Carcinogens Paper

Dear Paul:

Thanks for your edits. You have properly captured the issue that I (and Jane Caldwell) were musing about but didn't quite hit on the precise terminology. I like yours, and I think it describes precisely what that table is for. Perhaps the time on the plane being squished among the other passengers paid off. ☺

Sincerely,

David

David M. DeMarini, Ph.D.

Genetic Toxicologist

Integrated Systems Toxicology Division (B105-03)

U.S. Environmental Protection Agency

Research Triangle Park, NC 27711, USA

TEL 1 919 541 1510

FAX 1 919 541 0694

E-mail: demarini.david@epa.gov

Courier Address (Fed Ex., UPS, etc.)for DOCUMENTS

Dr. David M. DeMarini

US EPA (B105-03)

4930 Page Road

Durham, NC 27703, USA

Courier Address (Fed Ex., UPS, etc.)for CHEMICALS/SAMPLES

Dr. David M. DeMarini

Chemical Services A-184

US EPA

109 T.W. Alexander Drive

RTP, NC 27709, USA

From: Paul Lambert [<mailto:plambert@wisc.edu>]

Sent: Sunday, January 25, 2015 11:05 PM

To: Cogliano, Vincent

Cc: bucher@niehs.nih.gov; Martyn Smith; DeMarini, David; Chris Portier; Caldwell, Jane; Gibbons, Catherine; Kate Guyton; Fritz, Jason; iir@unc.edu; lambert@oncology.wisc.edu; Kavlock, Robert; hecht002@umn.edu; Robert Baan; Kurt Straif

Subject: Re: Revised Characteristics of Carcinogens Paper

Dear friends and colleagues.

Greetings from, of all places, Lyon, where I just arrived to participate on a review panel for one of the internal scientific components at the IARC. Being in severe jet lag mode driven by being relegated sardine status by IARC on my way over here, I am in the enviable position of having nothing better to do than to make life worse for all of you. So here is my two cents on the document.

What we identified were ten **biological/biochemical processes** that contribute to carcinogenesis. These are NOT mechanisms. There is no need to call them mechanisms if the word doesn't fit. The document reads like a person attending an alcohol anonymous meeting who is in denial that he is an alcoholic... *'We want to call these shared features of carcinogens 'mechanisms' though we understand they are not mechanisms, but we still want to call them mechanisms. So we will call them mechanisms'* Admit it folks, they are NOT mechanisms! If you want anyone to read and appreciate the importance of this discussion, lets get over the fact that we are not defining mechanisms, but rather the biological/biochemical properties of an agent that contribute to carcinogenesis and then get on with telling the reader why they are important.

If you agree with me, then my changes may make sense to you and you should read my edited version and consider whether the term I have applied is optimal or not. If you don't, then there is probably no value in your reading my version unless you too are suffering from insomnia or severe jet lag.

Best wishes,

Grumpy Paul

Paul F. Lambert, Ph.D.

Howard M Temin Professor and Chair of Oncology

Director, McArdle Laboratory for Cancer Research

University of Wisconsin School of Medicine and Public Health

Wisconsin Institutes for Medical Research, room 6459

1111 Highland Avenue

Madison, WI 53705-2275

tel: 608-262-8533 fax: 608-262-2824

email: plambert@wisc.edu